

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
RAYMOND A. MILLER
PEPPER HAMILTON LLP
500 GRANT STREET
ONE MELLON BANK CENTER, 50TH FLOOR
PITTSBURGH, PA 15219

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Applicant's or agent's file reference 112911.02802		Date of mailing (day/month/year) 11 SEP 2008 FOR FURTHER ACTION See paragraph 2 below
International application No. PCT/US07/81260	International filing date (day/month/year) 12 October 2007 (12.10.2007)	Priority date (day/month/year) 13 October 2006 (13.10.2006)
International Patent Classification (IPC) or both national classification and IPC IPC: G06F 19/00(2006.01);G06G 7/58(2006.01) USPC: 702/19,27;703/11		
Applicant THE TRUSTEES OF THE UNIVERSITY OF PRINCETON		

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	Date of completion of this opinion 12 August 2008 (12.08.2008)	Authorized officer SUZANNE M. NOAKES Telephone No. 571-272-1600
---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------	-------------------------------------------------------------------	-----------------------------------------------------------------------

Form PCT/ISA/237 (cover sheet) (April 2007)

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US07/81260

Box No. 1 Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of:

- ☒ the international application in the language in which it was filed
☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. ☐ This opinion has been established taking into account the rectification of an obvious mistake authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a)).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, this opinion has been established on the basis of:

a. type of material

- ☐ a sequence listing
☐ table(s) related to the sequence listing

b. format of material

- ☐ on paper
☐ in electronic form

c. time of filing/furnishing

- ☐ contained in the international application as filed.
☐ filed together with the international application in electronic form.
☐ furnished subsequently to this Authority for the purposes of search.

4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

5. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/US07/81260

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application
☒ claims Nos. 18-34

because:

- ☒ the said international application, or the said claim Nos. 18-34 relate to the following subject matter which does not require an international search (*specify*):

Applicants did not elect to pay the additional fees required to search the noted claims.

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____ are so unclear that no meaningful opinion could be formed (*specify*):

- ☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):

- ☒ no international search report has been established for said claims Nos. 18-34

- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).

- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/US97/81260

Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)

Claims NONE YES

Claims 1-17 NO

Inventive step (IS)

Claims NONE YES

Claims 1-17 NO

Industrial applicability (IA)

Claims 1-17 YES

Claims NONE NO

2. Citations and explanations:

Claims 1-17 lack novelty and an inventive step under PCT Article 33(2)&(3) as being anticipated by McCluskey et al. (Anti-Cancer Drug Design, 2001, 16:291-303) who teach a method of identifying a new class of protein phosphatase 2A inhibitor compounds by rationally designing said compounds by using the three-dimensional atomic coordinates of a modeled PP2A structure. The method utilizes the three-dimensional molecular modeling algorithm/program Cerius2-LigandFit (see p. 298, 1st column, Docking Studies; also see p. 294, 1st column, 1st two paragraphs) to ascertain the exact binding mode of candidate compounds numbers 24 and 25, which are synthesized compounds. It is noted that claims are drawn to product-by-process compounds wherein said process of generating said compounds does not necessarily impart novelty and an inventive step to said compound.

Claims 1-17 also lack novelty and an inventive step under PCT Article 33(2)&(3) as being anticipated by Sakoff & McCluskey (Curr. Pharm. Design, 2004, 10:1139-59) who teach many different PP2A compounds that are not aladeic acid or microcystin-LR, but which are analogues of these compounds and which inhibit PP2A (see Sections 3.1.1 (Table 1) and 3.1.3 (Table 4), respectively). Many other compounds are taught which also inhibit PP2A. See Sections 3.1.2 Tautomycins (and Tables 2 and 3); Section 3.1.4 Cantaridin; Section 3.1.5 Fostriecin. In addition, it also taught that PP2A and PP1 may have a common pharmacophore which is useful in the design and development new inhibitor compounds based on molecular modeling studies (see Section 3.1.6, 3.2, and all of Section 3.3). For instance, it is noted that the strategy used by Wpf et al. has led to the development of a common pharmacophore and as a result, 18 analogues have been developed and tested (see Section 3.3.6) which have greater than 50% inhibition at 100 μ M. It is noted that claims are drawn to product-by-process compounds wherein said process of generating said compounds does not necessarily impart novelty and an inventive step to said compound and thus the compounds as taught in Sakoff & McCluskey anticipate the instant claims.

Claims 1-17 meet the criteria set out in PCT Article 33(4), and thus possess industrial applicability because the subject matter claimed can be made or used in industry. The compounds of the instant claimed invention may be useful in the medical industry as potential therapeutic compounds.